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Case of the month: What's your diagnosis?

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Animal and gross pathological examination

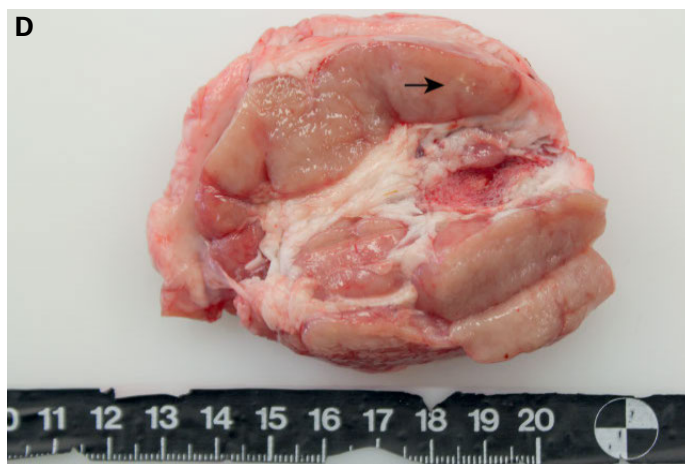
Two swine (A and B) slaughtered at different abattoirs were examined macroscopically during meat inspection. The carcass of the **fattening pig A** showed various organ lesions in liver, lung, spleen and mandibular and mesenteric lymph nodes. The liver was severely altered and replaced by a poorly demarcated, confluent and irregular beige parenchyma in which some unaffected areas of liver remained (Fig 1A). The lungs showed very small, up to 7 mm, polyhedral, raised and white regions on the

surface, which penetrated minimally into the deeper parenchyma (Fig 1B). Randomly distributed throughout the spleen, several variously-sized, from 0.5 to 1 cm big white nodules within the deeper parenchyma slightly raised over the surface (Fig 1C). Both mesenteric and mandibular lymph nodes exhibited multiple small foci of hard, white calcifications of 1 mm (Fig 1D).

The carcass of **animal B** (sow) revealed multiple bulging, well demarcated white to yellow masses of around



Figure 1: A: Liver of animal A (sow). View of a cut section through the liver parenchyma. The parenchyma is diffusely altered and showed irregular and poorly demarcated and coalescing, randomly distributed white to beige areas. B: Lungs of animal A. View of part of a lung lobe which showed multifocal slightly raised white nodular and poorly demarcated polyhedral areas of 9 x 6 x 5 mm in size. These nodular lesions were present in the pleura and deepened also into the parenchyma. C: Spleen of animal A with multiple nodular lesions. D: Lymph node of animal A showing small calcifications (arrow).



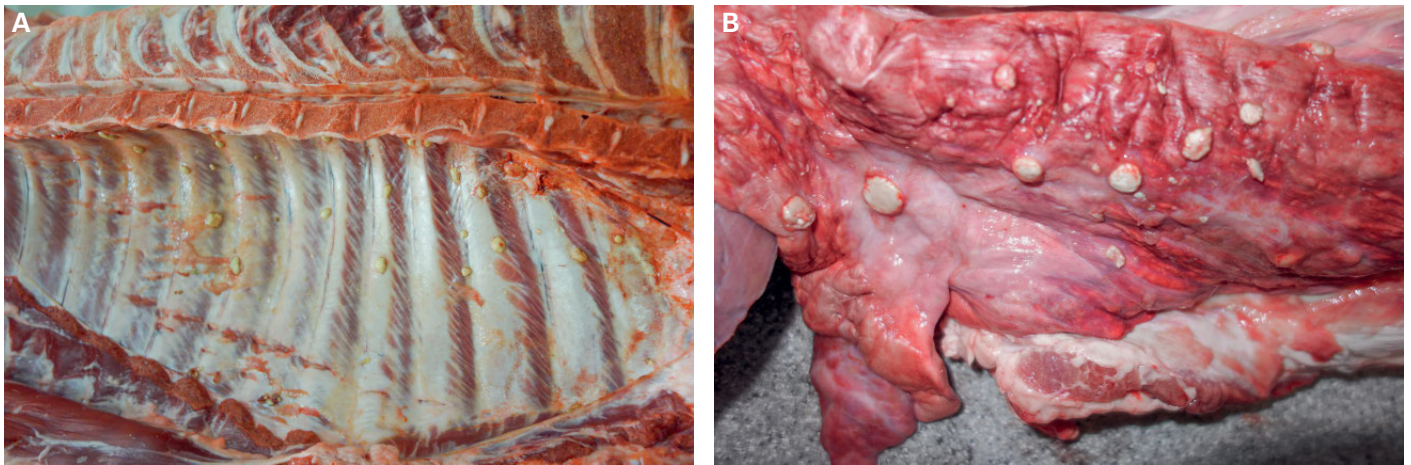


Figure 2: A: Pleura costalis of animal B (sow) with multiple nodular lesions. B: Pleura pulmonalis of pig B showing multiple nodular lesions.

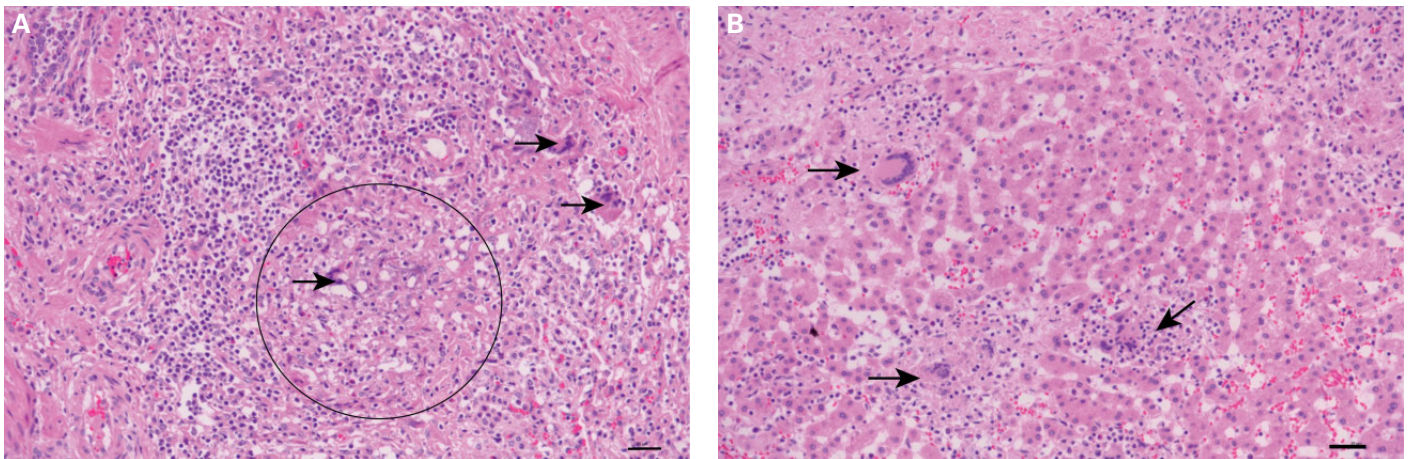


Figure 3: A: Tissue of the lung of animal A (sow), HE. Multiple granulomas (circle) disrupting the lung parenchyma with central epithelioid macrophages surrounded by variable amounts of lymphocytes and plasma cells. Note the numerous multinucleated giant cells (arrows) present centrally between the epithelioid macrophages and building a rim around it, bar=40µm. B: Liver of animal A (sow), HE. The liver architecture is disrupted by randomly distributed granulomatous lesions characterized by central loss of cellular detail and infiltration by numerous epithelioid macrophages surrounded by variable amounts of lymphocytes and plasma cells. Abundant multinucleated giant cells (arrows) are associated to the inflammatory component and are visible within the granulomas, bar=40µm.

1 × 1 × 1 cm on the pleura costalis (Fig 2A) and on the pleura pulmonalis (Fig 2B) which were randomly distributed. On the cut surface, the content of the nodules was friable to pasty and white-yellowish.

Histopathological examination

In all examined and affected organs (liver, lung, spleen and lymph nodes) the histological changes were similar. Multifocally the parenchyma of the spleen, lung and lymph node was randomly replaced by a granulomatous inflammation. These were composed of loss of cellular detail and instead infiltration by disorganized numerous epithelioid macrophages admixed with variable numbers of lymphocytes and plasma cells with few neutrophils and eosinophils. Intermingled abundant multinucleated giant cells of the Langhans type were present surrounding and centrally located within these lesions (Fig 3A). Within the lymph node, few acid-fast bacteria could be observed with Ziehl-Neelsen staining within

macrophages. Regarding the liver, the architecture of the lobules was severely disrupted and affected through a multifocal to coalescing, bridging replacement of the parenchyma by the same granulomatous lesion described in the spleen and in the lung (Fig 3B). The lesions were randomly distributed and were composed of central loss of cellular detail and infiltration by epithelioid macrophages with intermingled and surrounding lymphocytes and plasma cells, and abundant randomly distributed Langhans type-giant cells. Based on the Ziehl-Neelsen staining multiple intracytoplasmic acid-fast bacteria could be observed in multiple macrophages of the granulomas.

Based on the macroscopic findings during meat inspection and described histopathologic lesions, what is your differential diagnosis? How would you confirm your diagnosis and please formulate your histopathological diagnosis – then turn the page. →

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What's your diagnosis?

S. Peterhans et al.

Further examinations

Microbiological examinations

Sampled organs, including lymph nodes and liver from animal A and lung, liver, pleura and lymph nodes from animal B, were submitted for mycobacterial culture.⁴ Decontaminated material was stained with Ziehl-Neelsen and revealed acid-fast bacteria in both cases (Fig 4). Samples of swine B were tested negative for *Mycobacterium tuberculosis* complex members using artus® *M. tuberculosis* PCR Kit according to the manufacturer's protocol (QIAGEN, Hilden, Germany). Decontaminated material of animal A and B was enriched in liquid mycobacterial media (BACTEC MGIT 960 Mycobacterial Detection System; Becton Dickinson) at 37°C. Mycobacteria grew after one week of incubation. Subcultures were grown on Middlebrook 7H10 supplemented with PANTA (polymyxin B, amphotericin B, nalidixic acid, trimethoprim, azlocillin) antibiotic mixture (BD). Species identification was performed using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF-MS, Bruker Daltronics, Bremen, Germany) and revealed *Mycobacterium avium* ssp. *hominisuis* (MAH) as causative agent in both cases.

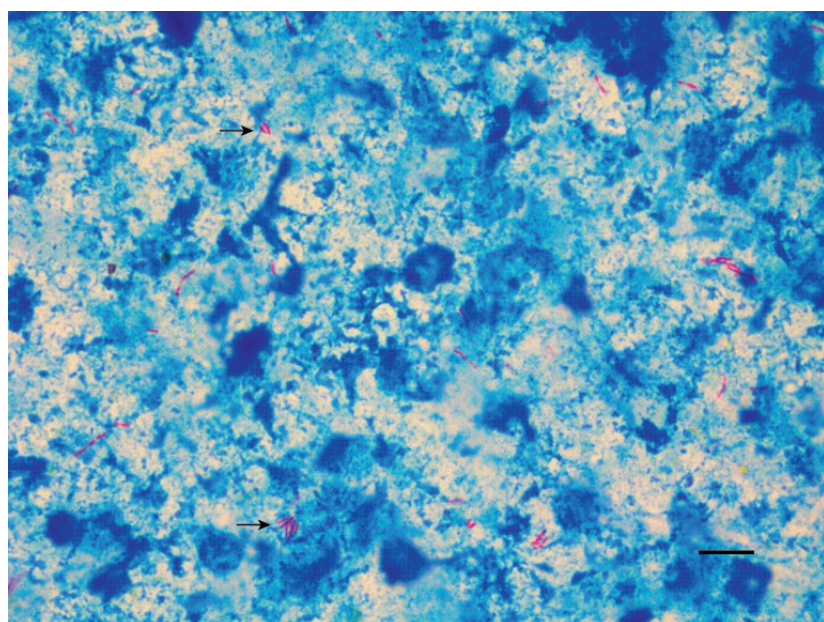


Figure 4: A: Ziehl-Neelsen staining of decontaminated material sampled from various organs of two swines showing acid fast bacilli (arrows), bar=10µm.

Diagnosis

Disease: Mycobacteriosis

Etiology: *Mycobacterium avium* ssp. *hominisuis*

Histopathological diagnosis: granulomatous hepatitis, pneumonia, splenitis and lymphadenitis (disseminated atypical mycobacteriosis/generalized atypical mycobacteriosis).

Discussion

The nontuberculous *Mycobacterium* MAH is a member of the *Mycobacterium avium* complex (MAC), which comprises several important bacterial subspecies, including *Mycobacterium avium* ssp. *avium*, the pathogen of avian tuberculosis, and *Mycobacterium avium* ssp. *paratuberculosis*, the agent of paratuberculosis.^{2,5} The designation 'hominisuis' underlines the two main host species of this NTM, namely humans and pigs.⁵ MAH acts as an opportunistic pathogen; however, infections in humans can lead to severe conditions, including pulmonary disease, lymphadenitis and disseminated infections in immunocompromised patients.² Swine are often subclinically infected and gross lesions are only detected during meat inspection in abattoirs. Except from sporadically reported reproductive disorders, there is no predisposition to severe clinical symptoms in pigs.³ The typical manifestation in subclinical cases comprises granulomatous lesions in mandibular lymph nodes and in lymph nodes and lymphatic tissues of the digestive tract with dissemination to liver and lungs. Due to a similar appearance, an infection with *Mycobacterium* (*M.*) *tuberculosis* complex members should be considered an important differential diagnosis and should always be ruled out.^{1,2} Swine B showed such distinct granulomatous lesions in the lungs and adjacent pleura and was sent to the Reference laboratory as a case of suspected tuberculosis. Macroscopic changes of swine A were more disseminated, however granulomatous macroscopic changes in lung, spleen and lymph nodes were suspicious for mycobacteriosis. Presence of acid-fast rod-shaped bacilli in Ziehl-Neelsen staining strengthened the suspicion of mycobacterial involvement in both cases and was confirmed by cultural detection of MAH.

MAH occurs ubiquitously in the environment and cases of human infections have been linked to water systems, saunas, pools and organic environmental materials.² In swine production bedding peat has been identified as natural MAH infection source. Subclinically infected pigs shed MAH through the fecal-oral

transmission route into the herd.¹ Affected pigs without any visible lesions at slaughter have been described and may pose a risk as source of infection for humans through consumption of insufficiently cooked pork meat.^{1,2,6} Meat inspection in abattoirs remains the most important tool for detection of mycobacteriosis and in particular tuberculosis.

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